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Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Iscalimab (CFZ533)

Trial Indication(s)

Sjögren's Syndrome

Protocol Number

CCFZ533B2201

Protocol Title

A 48-week, 6-arm, randomized, double-blind, placebo-controlled multicenter trial to assess the safety and efficacy of multiple CFZ533 doses administered subcutaneously in two distinct populations of patients with Sjogren's Syndrome (TWINSS)

Clinical Trial Phase

Phase 2

Phase of Drug Development

Phase IIb

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Study Start/End Dates

Study Start Date: October 01, 2019 (Actual)
Primary Completion Date: September 28, 2022 (Actual)
Study Completion Date: June 06, 2023 (Actual)

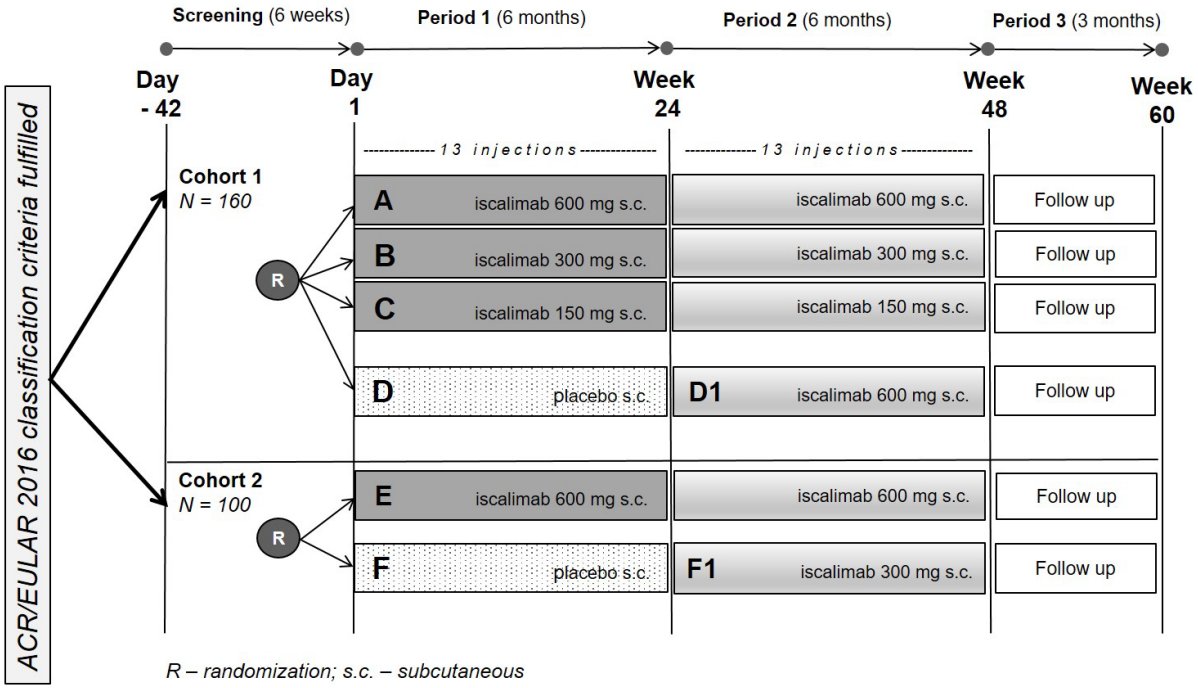
Reason for Termination (If applicable)

Not applicable

Study Design/Methodology

This study was a phase 2b, double-blind, randomized, placebo-controlled, dose-range finding trial to assess the efficacy, safety and tolerability of three doses of iscalimab (150, 300 and 600 mg) administered subcutaneous (s.c.) every 2 weeks, bi-weekly q2w after a short loading dose regimen in two populations with Sjögren's Syndrome (SjS):

- Cohort 1: subjects with moderate-to-severe systemic and symptomatic disease involvement.
- Cohort 2: subjects with low systemic disease involvement but high symptom burden.



R – randomization; s.c. – subcutaneous

Screening	Double-blind treatment Period 1		Double-blind treatment Period 2		Follow-up
6 weeks	24 weeks		24 weeks		12 weeks
	Loading regimen weekly	Maintenance Q2W	Loading regimen weekly	Maintenance Q2W	
	2 weeks (weekly visits)	22 weeks (visits every 2 wks)	2 weeks (weekly visits)	22 weeks (visits every 2 wks)	

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Centers

71 centers in 23 countries: Hungary(3), Australia(1), Japan(5), Turkey(1), Portugal(4), Greece(1), France(5), Russia(6), Germany(4), Israel(3), Austria(2), Italy(3), United States(8), United Kingdom(3), Brazil(3), Netherlands(2), Canada(3), Chile(5), Korea, Republic of(1), Romania(2), Argentina(2), Sweden(1), Colombia(3)

Objectives:

Objectives	**Endpoints**
Primary objectives	**Endpoints for primary objective(s)**
Cohort 1 ● To demonstrate a dose-response of CFZ533 (iscalimab) based on change in ESSDAI from baseline at Week 24.	**Cohort 1** ● Change in ESSDAI score from baseline at 24 weeks as compared to placebo.
Cohort 2 ● To estimate the effect of CFZ533 (iscalimab) 600 mg s.c. on the change in ESSPRI at Week 24.	**Cohort 2** ● Change in ESSPRI score from baseline at 24 weeks as compared to placebo.
Secondary objectives	**Endpoints for secondary objectives**
Cohort 1 ● To demonstrate a dose response of iscalimab based on change in ESSPRI from baseline at Week 24 ● To estimate the effects of iscalimab based on ● change in FACIT-F from baseline at Week 24 ● change in physician's global assessment (PhGA) from baseline at Week 24	**Cohort 1** ● Change from baseline in ● ESSPRI at Week 24 ● FACIT-F score at Week 24 ● PhGA overall disease activity scores at Week 24
● To assess ● the effect of iscalimab in the serum Free Light Chains (FLC) levels over time ● the changes in IgG and IgM levels over time after iscalimab treatment ● the effect of iscalimab on plasma CXCL-13 over time	● Serum FLC levels at analysis visit up to end of study ● IgG and IgM levels at analysis visits up to end of study ● Percent change from baseline in plasma CXCL-13 levels at analysis visits up to end of study

Objectives	Endpoints
Cohort 2 ● To estimate the effects of iscalimab based on changes in ● FACIT-F from baseline at Week 24 ● PhGA from baseline at Week 24 ● ESSDAI from baseline at Week 24 To evaluate the efficacy of iscalimab in improving the dry eye symptoms measured by IDEEL at Week 24 To assess ● the effect of iscalimab in the serum FLC levels over time ● the changes in IgG and IgM levels over time after iscalimab treatment ● the effect of iscalimab on plasma CXCL-13 over time	**Cohort 2** ● Change from baseline ● in FACIT-F score at Week 24 ● in PhGA (VAS) at Week 24 ● in ESSDAI at Week 24 ● Proportion of subjects with at least 12 points improvement on IDEEL dry eye symptom bother module score at Week 24 ● Serum FLC levels at analysis visits up to end of study ● IgG and IgM levels at analysis visits up to end of study ● Percent change from baseline in plasma CXCL-13 levels at analysis visits up to end of study
Cohort 1 & 2 ● To assess ● safety and tolerability of iscalimab ● immunogenicity of iscalimab ● the pharmacokinetics and dose-exposure relationship of iscalimab ● To measure soluble CD40 in plasma	**Cohort 1 & 2** ● Incidence of Treatment-emergent AEs (TEAEs) /Serious Adverse Events (SAEs) from baseline to Week 24 ● Incidence of TEAEs/SAEs from Week 24 to end of study ● Routine hematology and clinical chemistry laboratory test results at analysis visits up to end of study ● Vital signs at analysis visits up to end of study ● Incidence of anti- iscalimab antibodies in plasma at analysis visits up to end of study ● Free iscalimab concentration in plasma during the treatment (Ctrough) and follow-up (up to end of study) periods ● Free or total soluble CD40 in the absence or presence of iscalimab, respectively at analysis visits up to end of study

Test Product (s), Dose(s), and Mode(s) of Administration

- Iscalimab was provided in vials of 150 mg/1 mL as a solution for subcutaneous administration.
- Placebo was also provided in vials of 0 mg/1 mL as a solution for subcutaneous administration.

Statistical Methods

Cohort 1

The primary efficacy endpoint for Cohort 1 was to compare the dose-response of iscalimab (150, 300 or 600 mg s.c. Q2W) vs placebo based on change in ESSDAI from baseline at Week 24.

The following estimand framework was adopted:

- Population: Full Analysis Set (FAS)
- Variable of interest: Change from baseline in ESSDAI total score after 24 weeks of subcutaneous iscalimab administrations. This was defined as the baseline ESSDAI value minus the Week 24 ESSDAI value with positive values indicating improvement in disease status.
- Inter-current events: Potential inter-current events in the study that may have impacted on primary efficacy analysis of Cohort 1 included early discontinuation from the study treatment, interruption of study treatment, intensified symptomatic control treatment and intensified immunosuppressive treatment.
- Summary measure: Adjusted mean change from baseline in ESSDAI total score at Week 24 was calculated from MMRM (Mixed Model for Repeated Measures) at the dose levels of 0 mg (placebo), 150 mg, 300 mg and 600 mg.

Cohort 2

The primary efficacy endpoint for Cohort 2 was to compare the dose-response of iscalimab 600 mg s.c. Q2W vs placebo based on change in ESSPRI from baseline at Week 24.

The following estimand framework was adopted:

- Population: Full Analysis Set (FAS)
- Variable of interest: Response status defined as patients achieving at least 1 point or 15% improvement on ESSPRI total score at Week 24
- Inter-current events: Potential inter-current events in the study that may have impacted on primary efficacy analysis of Cohort 2 included early discontinuation from the study treatment, interruption of study treatment,

intensified symptomatic control treatment and intensified immunosuppressive treatment.

- Summary measure: Proportion of responders in placebo and iscalimab 600 mg arms.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

Both cohorts must have met all the following criteria:

1. Signed informed consent must be obtained prior to participation in the study
2. Male or female patient >= 18 years of age
3. Classification of Sjögren's Syndrome according to ACR/EULAR 2016 criteria (Shiboski et al 2016)
4. Seropositive for anti-Ro/SSA antibodies
5. Stimulated whole salivary flow rate of >= 0.1 mL/min
6. Able to communicate well with the Investigator to understand and comply with the requirements of the study

Inclusion criteria specific for Cohort 1:

7. Screening ESSDAI value >= 5 within the following 8 organ domains: constitutional, lymphadenopathy, glandular, articular, cutaneous, renal, hematologic and biologic

• Patients with involvement of one or more of the remaining 4 domains are eligible but scores of these domains will not contribute to the assessment for eligibility for Cohort 1

• At selected sites participating in Cohort 2, patients who based on the above criterion 7, do not qualify for Cohort 1, should be further evaluated for Cohort 2

8. Screening ESSPRI score of >= 5

Inclusion criteria specific for Cohort 2:

9. Screening ESSDAI value < 5 within 8 domains scored for inclusion criterion #7 Cohort 1

10. Screening ESSPRI fatigue subscore >= 5 or ESSPRI dryness subscore >= 5

11. Hypergammaglobulinemia defined by IgG greater than upper limit of normal (ULN) or lymphocytopenia (less than lower limit of normal (LLN)) or hypocomplementemia (low C3, or low C4 - when considered due to disease activity and not due to genetic factors)

12. Score of >= 30 on IDEEL symptom bother questionnaire at Screening

Exclusion Criteria:

1. Sjögren's Syndrome overlap syndromes where another autoimmune rheumatic disease constitutes the principal illness

2. Use of other investigational drugs within 5 half-lives of enrollment or within 30 days whichever is longer, or longer if required by local regulations

3. Prior treatment with any of the following within 6 months prior to randomization:

• B-cell depletors (e.g. rituximab, ianalumab) unless CD19+ B cell count have returned to ≥ 50 cells/µL

• abatacept

• anti-tumor necrosis factor alpha monoclonal anti-body

• intravenous/subcutaneous Ig; plasmapheresis; i.v. or oral cyclophosphamide

• i.v. or oral cyclosporine A

• any other immunosuppressants unless explicitly allowed in criterion #5

4. Use of steroids (predniso(lo)ne or equivalent corticosteroid) at dose > 10 mg/day

5. Use of steroids and synthetic DMARDS at inconsistent dose and within 3 months prior to randomization

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Participant Flow Table

Period 1 (up to Week 24): Cohorts 1&2

	Cohort 1 / Arm D (Period 1): Placebo	Cohort 1/Arm C: CFZ533 150 mg	Cohort 1/Arm B: CFZ533 300 mg	Cohort 1/Arm A: CFZ533 600 mg	Cohort 1 / Arm D1 (Period 2): CFZ533 600mg (from Week 24)	Cohort 2/Arm F: Placebo	Cohort 2/Arm E: CFZ533 600 mg	Cohort 2 / Arm F1 (Period 2): CFZ533 300mg	Total
Arm/Group Description	Placebo treatment is administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2 to Week 22 in Period 1.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 150 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 150 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 300 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 300 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Weeks 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	3 weekly subcutaneous (s.c.) loading doses of 600 mg iscalimab on Week 24, 25 and 26. After Week 26 and up to Week 46 (last dose), iscalimab was administered bi-weekly at 600 mg.	Placebo treatment was administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2 to Week 22 in Period 1.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	3 weekly subcutaneous (s.c.) loading doses of iscalimab: 600 mg on Week 24, and 300 mg on Week 25 and Week 26. After Week 26, iscalimab was administered s.c. bi-weekly at 300 mg.	
Started	43	44	43	43	0	50	50	0	273
Full analysis set (FAS)	43	44	43	43	0	50	50	0	273

Safety Set (SAF)	43	44	42	44	0	50	50	0	273
Continued to Treatment Period 2	41	42	41	39	0	45	48	0	256
Completed	41	42	41	39	0	44	48	0	255
Not Completed	2	2	2	4	0	6	2	0	18
Adverse Event	1	1	2	4	0	3	1	0	12
Lost to Follow-up	1	0	0	0	0	0	0	0	1
Physician Decision	0	1	0	0	0	0	0	0	1
Subject decision	0	0	0	0	0	3	1	0	4

Period 2 (up to Week 48): Cohorts 1&2

	Cohort 1 / Arm D (Period 1): Placebo	**Cohort 1/Arm C: CFZ533 150 mg**	**Cohort 1/Arm B: CFZ533 300 mg**	**Cohort 1/Arm A: CFZ533 600 mg**	**Cohort 1 / Arm D1 (Period 2): CFZ533 600mg (from Week 24)**	**Cohort 2/Arm F: Placebo**	**Cohort 2/Arm E: CFZ533 600 mg**	**Cohort 2 / Arm F1 (Period 2): CFZ533 300mg**	**Total**
Arm/Group Description	Placebo treatment is administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 150 mg on Week 1 and Week 2.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 300 mg on Week 1 and Week 2.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Weeks 0, 1 and 2. From Week 2 and up to Week	3 weekly subcutaneous (s.c.) loading doses of 600 mg iscalimab on Week 24, 25 and 26. After Week 26 and up to Week 46 (last	Placebo treatment was administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, 1 and 2. From Week 2 and up to Week	3 weekly subcutaneous (s.c.) loading doses of iscalimab: 600 mg on Week 24, and 300 mg on Week 25 and Week 26.	

	to Week 22 in Period 1.	From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 150 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 300 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	dose), iscalimab was administered bi-weekly at 600 mg.	to Week 22 in Period 1.	46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	After Week 26, iscalimab was administered s.c. bi-weekly at 300 mg.	
Started	0	42	41	39	41	0	48	45	256
Continued to Post-Treatment Follow-up Period	0	42	40	39	41	0	46	45	253
Completed	0	38	36	39	39	0	41	44	237
Not Completed	0	4	5	0	2	0	7	1	19
Adverse Event	0	1	1	0	0	0	1	1	4
Death	0	0	1	0	0	0	1	0	2
Physician Decision	0	0	1	0	0	0	0	0	1
Subject decision	0	3	1	0	2	0	4	0	10
Withdrawal of Consent	0	0	1	0	0	0	0	0	1
Protocol deviation	0	0	0	0	0	0	1	0	1

Baseline Characteristics

	Cohort 1 / Arm D (Period 1): Placebo	Cohort 1/Arm C: CFZ533 150 mg	Cohort 1/Arm B: CFZ533 300 mg	Cohort 1/Arm A: CFZ533 600 mg	Cohort 1 / Arm D1 (Period 2): CFZ533 600mg (from Week 24)	Cohort 2/Arm F: Placebo	Cohort 2/Arm E: CFZ533 600 mg	Cohort 2 / Arm F1 (Period 2): CFZ533 300mg	Total
Arm/Group Description	Placebo treatment is administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2 to Week 22 in Period 1.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 150 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 150 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 300 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 300 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Weeks 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	3 weekly subcutaneous (s.c.) loading doses of 600 mg iscalimab on Week 24, 25 and 26. After Week 26 and up to Week 46 (last dose), iscalimab was administered bi-weekly at 600 mg.	Placebo treatment was administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2 to Week 22 in Period 1.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	3 weekly subcutaneous (s.c.) loading doses of iscalimab: 600 mg on Week 24, and 300 mg on Week 25 and Week 26. After Week 26, iscalimab was administered s.c. bi-weekly at 300 mg.	
Number of Participants [units:	43	44	43	43	0	50	50	0	273

participants]									
Baseline Analysis Population Description	Demographics and Baseline Characteristics were assessed in Period 1.								
Age Continuous (units: Years) Analysis Population Type: Participants Mean ± Standard Deviation									
	53.3±9.55	49.3±14.41	48.7±12.78	52.6±12.31		49.4±13.40	53.6±13.18		51.2±12.61
Sex: Female, Male (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)									
Female	41	42	41	40	0	48	50	0	262
Male	2	2	2	3	0	2	0	0	11
Race (NIH/OMB) (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)									
American Indian or Alaska Native	0	1	1	1	0	0	1	0	4
Asian	3	4	4	5	0	7	8	0	31
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0
Black or African American	1	1	2	1	0	3	3	0	11

White	38	37	35	35	0	38	37	0	220
More than one race	1	1	1	1	0	1	0	0	5
Unknown or Not Reported	0	0	0	0	0	1	1	0	2

Primary Outcome Result(s)

Cohort 1: Change in EULAR Sjögren Syndrome Disease Activity Index (ESSDAI) score from baseline at 24 weeks as compared to placebo

Description	ESSDAI is a validated disease outcome measure for SjS that contains 12 organ-specific domains contributing to disease activity. For each domain, features of disease activity are scored in 3 or 4 levels according to their severity. These scores are then summed across the 12 domains in a weighted manner to provide the total score. The domains (weights) are as follows: constitutional (3), lymphadenopathy (4), glandular (2), articular (2), cutaneous (3), pulmonary (5), renal (5), muscular (6), peripheral nervous system (PNS) (5), central nervous system (CNS) (5), hematological (2) and biological (1). The total score may vary between 0-123. It is considered low activity an ESSDAI < 5; moderate activity 5-13, and high activity if ESSDAI is >= 14.
Time Frame	Baseline, Week 24
Analysis Population Description	Full Analysis Set. Only participants in cohort 1 with a value at both Baseline and post-baseline visit included.

	Cohort 1 / Arm D (Period 1): Placebo	**Cohort 1/Arm C: CFZ533 150 mg**	**Cohort 1/Arm B: CFZ533 300 mg**	**Cohort 1/Arm A: CFZ533 600 mg**
Arm/Group Description	Placebo treatment is administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2 to Week 22 in Period 1.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 150 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 300 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Weeks 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-

		administered s.c. bi-weekly at 150 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	administered s.c. bi-weekly at 300 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.
Number of Participants Analyzed [units: participants]	41	42	41	39
Cohort 1: Change in EULAR Sjögren Syndrome Disease Activity Index (ESSDAI) score from baseline at 24 weeks as compared to placebo (units: Unit on a scale)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
	-4.0 ± 0.73	-7.0 ± 0.70	-5.4 ± 0.71	-6.9 ± 0.73

Statistical Analysis

Groups	Cohort 1 / Arm D (Period 1): Placebo, Cohort 1/Arm C: CFZ533 150 mg	ESSDAI score from baseline at 24 weeks as compared to placebo - Cohort 1
Type of Statistical Test	Other	
P Value	0.0025	
Method	Mixed Models Analysis	
Other LS Mean difference CFZ533-Placebo	-3.0	MMRM that includes treatment, visit, treatment by visit interaction, stratification factor baseline ESSDAI score (< 10 or >= 10 based on weighted scores), and region as factors and baseline value of corresponding parameter as continuous covariates.
95 % Confidence Interval	-4.9 to -1.1	

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Statistical Analysis

Groups	Cohort 1 / Arm D (Period 1): Placebo, Cohort 1/Arm B: CFZ533 300 mg	ESSDAI score from baseline at 24 weeks as compared to placebo - Cohort 1
Type of Statistical Test	Other	
P Value	0.1578	
Method	Mixed Models Analysis	
Other LS Mean difference CFZ533-Placebo	-1.4	MMRM that includes treatment, visit, treatment by visit interaction, stratification factor baseline ESSDAI score (< 10 or >= 10 based on weighted scores), and region as factors and baseline value of corresponding parameter as continuous covariates.
95 % Confidence Interval	-3.3 to 0.5	

Statistical Analysis

Groups	Cohort 1 / Arm D (Period 1): Placebo, Cohort 1/Arm A: CFZ533 600 mg	ESSDAI score from baseline at 24 weeks as compared to placebo - Cohort 1
Type of Statistical Test	Other	
P Value	0.0037	
Method	Mixed Models Analysis	
Other LS Mean difference CFZ533-Placebo	-2.9	MMRM that includes treatment, visit, treatment by visit interaction, stratification factor baseline ESSDAI score (< 10 or >= 10 based on weighted scores), and region as factors and baseline value of corresponding parameter as continuous covariates.

95 % Confidence Interval 2-Sided	-4.9 to -1.0

Cohort 2: Change in EULAR Sjögren Syndrome Patient Reported Index (ESSPRI) score from baseline at 24 weeks as compared to placebo.

Description	The ESSPRI is a self-evaluation index for measuring symptoms including pain, fatigue and dryness. Each symptom was measured with a single 0 (no symptoms) to 10 (severe symptoms) numerical scale and the final ESSPRI score is calculated by averaging these domains with a maximum severity score of 10.
Time Frame	Baseline, Week 24
Analysis Population Description	Full Analysis Set. Only participants in cohort 2 with a value at both Baseline and post-baseline visit included.

	Cohort 2/Arm F: Placebo	Cohort 2/Arm E: CFZ533 600 mg
Arm/Group Description	Placebo treatment was administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2 to Week 22 in Period 1.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.
Number of Participants Analyzed [units: participants]	45	49
Cohort 2: Change in EULAR Sjögren Syndrome Patient Reported Index (ESSPRI) score from baseline at 24 weeks as compared to placebo. (units: Unit on a scale)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
	-1.21 ± 0.271	-1.79 ± 0.258

Statistical Analysis

Groups	Cohort 2/Arm F: Placebo, Cohort 2/Arm E: CFZ533 600 mg	ESSPRI score from baseline at 24 weeks as compared to placebo - Cohort 2
Type of Statistical Test	Other	
P Value	0.1210	
Method	Mixed Models Analysis	
Other LS Mean difference CFZ533-Placebo	-0.57	MMRM that includes treatment, visit, treatment by visit interaction and region as factors and baseline value of corresponding parameter as continuous covariates.
95 % Confidence Interval 2-Sided	-1.30 to 0.15	

Secondary Outcome Result(s)

Cohort 1: Change from baseline in ESSPRI at Week 24

Description	The ESSPRI is a self-evaluation index for measuring symptoms including pain, fatigue and dryness. Each symptom was measured with a single 0 (no symptoms) to 10 (severe symptoms) numerical scale and the final ESSPRI score is calculated by averaging these domains with a maximum severity score of 10.
Time Frame	Baseline, Week 24
Analysis Population Description	Full Analysis Set. Only participants in cohort 1 with a value at both Baseline and post-baseline visit included.

	Cohort 1 / Arm D (Period 1): Placebo	Cohort 1/Arm C: CFZ533 150 mg	Cohort 1/Arm B: CFZ533 300 mg	Cohort 1/Arm A: CFZ533 600 mg
Arm/Group Description	Placebo treatment is administered	3 weekly subcutaneous (s.c.) loading doses of	3 weekly subcutaneous (s.c.) loading doses of	3 weekly subcutaneous (s.c.) loading doses of

	subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2 to Week 22 in Period 1.	iscalimab were 600 mg on Week 0, and 150 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 150 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	iscalimab were 600 mg on Week 0, and 300 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 300 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	iscalimab were 600 mg on Weeks 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.
Number of Participants Analyzed [units: participants]	39	42	40	39
Cohort 1: Change from baseline in ESSPRI at Week 24 (units: Unit on a scale)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
	-1.3 ± 0.31	-1.8 ± 0.30	-1.6 ± 0.31	-1.8 ± 0.31

Statistical Analysis

Groups	Cohort 1 / Arm D (Period 1): Placebo, Cohort 1/Arm C: CFZ533 150 mg	ESSPRI at Week 24 - Cohort 1
Type of Statistical Test	Other	
P Value	0.2078	
Method	Mixed Models Analysis	
Other LS Mean difference CFZ533-Placebo	-0.5	MMRM that includes treatment, visit, treatment by visit interaction, stratification factor baseline ESSDAI score (< 10 or >= 10 based on weighted scores), and region as factors and baseline value of corresponding parameter as continuous covariates.

95 % Confidence Interval 2-Sided	-1.4 to 0.3	

Statistical Analysis

Groups	Cohort 1 / Arm D (Period 1): Placebo, Cohort 1/Arm B: CFZ533 300 mg	ESSPRI at Week 24 - Cohort 1
Type of Statistical Test	Other	
P Value	0.5132	
Method	Mixed Models Analysis	
Other LS Mean difference CFZ533-Placebo	-0.3	MMRM that includes treatment, visit, treatment by visit interaction, stratification factor baseline ESSDAI score (< 10 or >= 10 based on weighted scores), and region as factors and baseline value of corresponding parameter as continuous covariates.
95 % Confidence Interval 2-Sided	-1.1 to 0.6	

Statistical Analysis

Groups	Cohort 1 / Arm D (Period 1): Placebo, Cohort 1/Arm A: CFZ533 600 mg	ESSPRI at Week 24 - Cohort 1
Type of Statistical Test	Other	
P Value	0.1998	
Method	Mixed Models Analysis	
Other LS Mean difference CFZ533-Placebo	-0.5	MMRM that includes treatment, visit, treatment by visit interaction, stratification factor baseline ESSDAI score (< 10 or >= 10 based on weighted scores), and region as factors and baseline value

		of corresponding parameter as continuous covariates.
0.1998 % Confidence Interval 2-Sided	-1.4 to 0.3	

Cohort 1: Change from baseline in score of Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F) questionnaire at Week 24

Description	The Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-F version 4) is a 13-item, easy-to-administer tool that measures an individual's level of fatigue during their usual daily activities over the past week. The level of fatigue was measured on a 5-point Likert scale (0 = not at all, 1 = a little bit, 2 = somewhat, 3 = quite a bit, 4 = very much) except 2 items which were reversed scored. Final score range is 0-52 with lower scores indicating severe fatigue.
Time Frame	Baseline, 24 weeks
Analysis Population Description	Full Analysis Set. Only participants in cohort 1 with a value at both Baseline and post-baseline visit included.

	Cohort 1 / Arm D (Period 1): Placebo	Cohort 1/Arm C: CFZ533 150 mg	Cohort 1/Arm B: CFZ533 300 mg	Cohort 1/Arm A: CFZ533 600 mg
Arm/Group Description	Placebo treatment is administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2 to Week 22 in Period 1.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 150 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 150 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 300 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 300 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Weeks 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.
Number of Participants Analyzed [units: participants]	40	42	40	39

Cohort 1: Change from baseline in score of Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F) questionnaire at Week 24 (units: Unit on a scale)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
	7.0 ± 1.48	8.6 ± 1.45	8.0 ± 1.47	10.3 ± 1.50

Statistical Analysis

Groups	Cohort 1 / Arm D (Period 1): Placebo, Cohort 1/Arm C: CFZ533 150 mg	FACIT-F at Week 24 - Cohort 1
Type of Statistical Test	Other	
P Value	0.4363	
Method	Mixed Models Analysis	
Other LS Mean difference CFZ533-Placebo	1.6	MMRM that includes treatment, visit, treatment by visit interaction, stratification factor baseline ESSDAI score (< 10 or >= 10 based on weighted scores), and region as factors and baseline value of corresponding parameter as continuous covariates.
95 % Confidence Interval 2-Sided	-2.4 to 5.6	

Statistical Analysis

Groups	Cohort 1 / Arm D (Period 1): Placebo, Cohort 1/Arm B: CFZ533 300 mg	FACIT-F at Week 24 - Cohort 1
Type of Statistical Test	Other	
P Value	0.6181	
Method	Mixed Models Analysis	

Other LS Mean difference CFZ533-Placebo	1.0	MMRM that includes treatment, visit, treatment by visit interaction, stratification factor baseline ESSDAI score (< 10 or >= 10 based on weighted scores), and region as factors and baseline value of corresponding parameter as continuous covariates.
95 % Confidence Interval 2-Sided	-3.0 to 5.0	

Statistical Analysis

Groups	Cohort 1 / Arm D (Period 1): Placebo, Cohort 1/Arm A: CFZ533 600 mg	FACIT-F at Week 24 - Cohort 1
Type of Statistical Test	Other	
P Value	0.1050	
Method	Mixed Models Analysis	
Other LS Mean difference CFZ533-Placebo	3.3	MMRM that includes treatment, visit, treatment by visit interaction, stratification factor baseline ESSDAI score (< 10 or >= 10 based on weighted scores), and region as factors and baseline value of corresponding parameter as continuous covariates.
95 % Confidence Interval 2-Sided	-0.7 to 7.3	

Cohort 1: Change from baseline in Physician Global Assessment (PhGA) at Week 24

Description	Physician's global assessment (PhGA) of disease activity was performed using a Visual Analog Scale (VAS) - an unnumbered 100 mm horizontal line ranging from "no disease activity" (score 0) to "maximal disease activity" (score 100). The assessment of patient's condition on the day is made by placing a vertical mark across the line.
Time Frame	Baseline, 24 weeks

Analysis Population Description	Full Analysis Set. Only participants in cohort 1 with a value at both Baseline and post-baseline visit included.

	Cohort 1 / Arm D (Period 1): Placebo	Cohort 1/Arm C: CFZ533 150 mg	Cohort 1/Arm A: CFZ533 600 mg	Cohort 1/Arm B: CFZ533 300 mg
Arm/Group Description	Placebo treatment is administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2 to Week 22 in Period 1.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 150 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 150 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Weeks 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 300 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 300 mg. To maintain blinding in Period 2, placebo was administered at Week 25.
Number of Participants Analyzed [units: participants]	36	40	39	35
Cohort 1: Change from baseline in Physician Global Assessment (PhGA) at Week 24 (units: Unit on a scale)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
	-23.9 ± 2.94	-31.6 ± 2.83	-27.0 ± 2.87	-30.8 ± 3.00

Statistical Analysis

Groups	Cohort 1 / Arm D (Period 1): Placebo, Cohort 1/Arm C: CFZ533 150 mg	PhGA at Week 24 - Cohort 1
Type of Statistical Test	Other	
P Value	0.0561	

Method	Mixed Models Analysis	
Other LS Mean difference CFZ533-Placebo	-7.7	MMRM that includes treatment, visit, treatment by visit interaction, stratification factor baseline ESSDAI score (< 10 or >= 10 based on weighted scores), and region as factors and baseline value of corresponding parameter as continuous covariates.
95 % Confidence Interval 2-Sided	-15.6 to 0.2	

Statistical Analysis

Groups	Cohort 1 / Arm D (Period 1): Placebo, Cohort 1/Arm A: CFZ533 600 mg	PhGA at Week 24 - Cohort 1
Type of Statistical Test	Other	
P Value	0.4433	
Method	Mixed Models Analysis	
Other LS Mean difference CFZ533-Placebo	-3.1	MMRM that includes treatment, visit, treatment by visit interaction, stratification factor baseline ESSDAI score (< 10 or >= 10 based on weighted scores), and region as factors and baseline value of corresponding parameter as continuous covariates.
95 % Confidence Interval 2-Sided	-11.0 to 4.8	

Statistical Analysis

Groups	Cohort 1 / Arm D (Period 1): Placebo, Cohort 1/Arm B: CFZ533 300 mg	PhGA at Week 24 - Cohort 1
Type of Statistical Test	Other	

P Value	0.0974	
Method	Mixed Models Analysis	
Other LS Mean difference CFZ533-Placebo	-6.9	MMRM that includes treatment, visit, treatment by visit interaction, stratification factor baseline ESSDAI score (< 10 or >= 10 based on weighted scores), and region as factors and baseline value of corresponding parameter as continuous covariates.
95 % Confidence Interval 2-Sided	-15.0 to 1.3	

Cohort 2: Change from baseline in score of Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F) questionnaire at Week 24

Description	The Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-F version 4) is a 13-item, easy-to-administer tool that measures an individual's level of fatigue during their usual daily activities over the past week. The level of fatigue was measured on a 5-point Likert scale (0 = not at all, 1 = a little bit, 2 = somewhat, 3 = quite a bit, 4 = very much) except 2 items which were reversed scored. Final score range is 0-52 with lower scores indicating severe fatigue.
Time Frame	Baseline, 24 weeks
Analysis Population Description	Full Analysis Set. Only participants in cohort 2 with a value at both Baseline and post-baseline visit included.

	Cohort 2/Arm F: Placebo	**Cohort 2/Arm E: CFZ533 600 mg**
Arm/Group Description	Placebo treatment was administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2 to Week 22 in Period 1.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.
Number of Participants Analyzed [units: participants]	45	49

Cohort 2: Change from baseline in score of Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F) questionnaire at Week 24 (units: Unit on a scale)	Least Squares Mean ± Standard Error	Least Squares Mean ± Standard Error
	5.7 ± 1.32	7.3 ± 1.25

Statistical Analysis

Groups	Cohort 2/Arm F: Placebo, Cohort 2/Arm E: CFZ533 600 mg	FACIT-F at Week 24 - Cohort 2
Type of Statistical Test	Other	
P Value	0.3675	
Method	Mixed Models Analysis	
Other LS Mean difference CFZ533-Placebo	1.6	MMRM that includes treatment, visit, treatment by visit interaction and region as factors and baseline value of corresponding parameter as continuous covariates.
95 % Confidence Interval 2-Sided	-1.9 to 5.1	

Cohort 2: Change from baseline in Physician Global Assessment (PhGA) at Week 24

Description	Physician's global assessment (PhGA) of disease activity was performed using a Visual Analog Scale (VAS) - an unnumbered 100 mm horizontal line ranging from "no disease activity" (score 0) to "maximal disease activity" (score 100). The assessment of patient's condition on the day is made by placing a vertical mark across the line.
Time Frame	Baseline, 24 weeks
Analysis Population Description	Full Analysis Set. Only participants in cohort 2 with a value at both Baseline and post-baseline visit included.

	Cohort 2/Arm F: Placebo	Cohort 2/Arm E: CFZ533 600 mg
Arm/Group Description	Placebo treatment was administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2 to Week 22 in Period 1.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.
Number of Participants Analyzed [units: participants]	45	46
Cohort 2: Change from baseline in Physician Global Assessment (PhGA) at Week 24 (units: Unit on a scale)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
	-10.4 ± 2.37	-15.8 ± 2.29

Statistical Analysis

Groups	Cohort 2/Arm F: Placebo, Cohort 2/Arm E: CFZ533 600 mg	PhGA at Week 24 - Cohort 2
Type of Statistical Test	Other	
P Value	0.1014	
Method	Mixed Models Analysis	
Other LS Mean difference CFZ533-Placebo	-5.4	MMRM that includes treatment, visit, treatment by visit interaction and region as factors and baseline value of corresponding parameter as continuous covariates.
95 % Confidence Interval 2-Sided	-11.8 to 1.1	

Cohort 2: Change from baseline in ESSDAI at Week 24

Description	ESSDAI is a validated disease outcome measure for SjS that contains 12 organ-specific domains contributing to disease activity. For each domain, features of disease activity are scored in 3 or 4 levels according to their severity. These scores are then summed across the 12 domains in a weighted manner to provide the total score. The domains (weights) are as follows: constitutional (3), lymphadenopathy (4), glandular (2), articular (2), cutaneous (3), pulmonary (5), renal (5), muscular (6), peripheral nervous system (PNS) (5), central nervous system (CNS) (5), hematological (2) and biological (1). The final score may vary between 0-123. It is considered low activity an ESSDAI < 5; moderate activity 5-13, and high activity if ESSDAI is >= 14.
Time Frame	Baseline, week 24
Analysis Population Description	Full Analysis Set. Only participants in cohort 2 with a value at both Baseline and post-baseline visit included.

	Cohort 2/Arm F: Placebo	**Cohort 2/Arm E: CFZ533 600 mg**
Arm/Group Description	Placebo treatment was administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2 to Week 22 in Period 1.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.
Number of Participants Analyzed [units: participants]	45	47
Cohort 2: Change from baseline in ESSDAI at Week 24 (units: Unit on a scale)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
	0.2 ± 0.33	-0.3 ± 0.32

Statistical Analysis

Groups	Cohort 2/Arm F: Placebo, Cohort 2/Arm E: CFZ533 600 mg	ESSDAI at Week 24 - Cohort 2
Type of Statistical Test	Other	
P Value	0.2694	

Method	Mixed Models Analysis	
Other LS Mean difference CFZ533-Placebo	-0.5	MMRM that includes treatment, visit, treatment by visit interaction and region as factors and baseline value of corresponding parameter as continuous covariates.
95 % Confidence Interval 2-Sided	-1.4 to 0.4	

Cohort 2: Proportion of subjects with at least 12 points improvement measured by score of Impact of Dry Eye on Everyday Life (IDEEL) questionnaire symptom bother module at Week 24.

Description	The Impact of Dry Eye on Everyday Life (IDEEL) questionnaire is a comprehensive dry eye specific questionnaire to evaluate treatment satisfaction, symptom-related bother and impact on daily life in a population with dry eye. This study only utilized the Dry Eye Symptom-Bother module. The Dry Eye Symptom-Bother module of IDEEL is composed of a single dimension (20 items). A 4-point Likert-like scale is used: from “not at all” to “very much”. Patients could also answer “I did not have this symptom / Not applicable”. One item is scored on a 5-point Likert-like scale from “none of the time” to “all of the time”. The range for the symptom-bother score is 0 to 100, with higher scores indicating greater symptom bother.
Time Frame	Baseline, Week 24
Analysis Population Description	Full Analysis Set.

	Cohort 2/Arm F: Placebo	**Cohort 2/Arm E: CFZ533 600 mg**
Arm/Group Description	Placebo treatment was administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2 to Week 22 in Period 1.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.
Number of Participants Analyzed [units: participants]	50	50

Cohort 2: Proportion of subjects with at least 12 points improvement measured by score of Impact of Dry Eye on Everyday Life (IDEEL) questionnaire symptom bother module at Week 24. (units: Participants)	Count of Participants (Not Applicable)	Count of Participants (Not Applicable)
	20 (40%)	24 (48%)

Statistical Analysis

Groups	Cohort 2/Arm F: Placebo, Cohort 2/Arm E: CFZ533 600 mg	IDEEL using non-responder imputation up to Week 24 - Cohort 2 (Full Analysis Set)
Type of Statistical Test	Other	
P Value	0.5459	
Method	Fisher Exact	
Other Clopper-Pearson method	8.0	Difference CFZ533-Placebo
95 % Confidence Interval 2-Sided	-11.4 to 27.4	

Cohort 1: Incidence of adverse events (AEs), serious adverse events (SAEs) up to Week 24

Description	The distribution of adverse events in Treatment Period 1 was done via the analysis of frequencies for treatment emergent Adverse Event (TEAEs), Serious Adverse Event (TESAEs) and Deaths due to AEs, through the monitoring of relevant clinical and laboratory safety parameters. Analyses of data in the Safety Set (SAF) up to Week 24 (Period 1) is presented by actual treatment during Period 1, with data from separate cohort for the CFZ533 600mg and for the Placebo groups: CFZ533 600 mg, CFZ533 300 mg, CFZ533 150 mg and placebo.
Time Frame	Up to Week 24
Analysis Population Description	Safety Set (SAF).

	Cohort 1: Placebo	Cohort 1: CFZ533 150 mg	Cohort 1/Arm B: CFZ533 300 mg	Cohort 1: CFZ533 600 mg
Arm/Group Description	Cohort 1: Placebo	Cohort 1: CFZ533 150 mg	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 300 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 300 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	Cohort 1: CFZ533 600 mg
Number of Participants Analyzed [units: participants]	43	44	42	44
Cohort 1: Incidence of adverse events (AEs), serious adverse events (SAEs) up to Week 24 (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Death	0 (%)	0 (%)	0 (%)	0 (%)
Adverse Event	31 (72.09%)	38 (86.36%)	32 (76.19%)	35 (79.55%)
Serious Adverse Event	1 (2.33%)	1 (2.27%)	3 (7.14%)	4 (9.09%)
AE leading to study medication discontinuation	1 (2.33%)	1 (2.27%)	1 (2.38%)	5 (11.36%)

Cohort 1: Incidence of adverse events (AEs), serious adverse events (SAEs) in all Study Periods

Description The distribution of adverse events was done via the analysis of frequencies for treatment emergent Adverse Event (TEAEs), Serious Adverse Event (TESAEs) and Deaths due to AEs, through the monitoring of relevant clinical and laboratory safety parameters. Analyses of data in the Safety Set (SAF) for period 2/3 or overall study is presented by actual treatment sequence during periods 1 and 2, where the CFZ533 600 mg – CFZ533 600 mg sequence included data from patients in separate cohort. CFZ533 600 mg 24 Weeks arm includes only patients from Placebo – CFZ533 600 mg arm, who took at least one CFZ533 600 mg dose in Period 2 (Patients who received Placebo in Period 1 and

discontinued before Week 24 are not included). CFZ533 600 mg 48 Weeks arm includes all subjects from CFZ533 600 mg - CFZ533 600 mg arm, and subjects from CFZ533 150 mg - CFZ533 150 mg and CFZ533 300 mg - CFZ533 300 mg arms but only took the first or the first two loading dose(s) in period 1.

Time Frame: up to 14 weeks following the last dose of study treatment, up to maximum Week 60

Analysis Population Description: Safety Set (SAF).

	Cohort 1: CFZ533 600 mg 24 Weeks	**Cohort 1: CFZ533 150 mg 48 Weeks**	**Cohort 1: CFZ533 300 mg 48 Weeks**	**Cohort 1: CFZ533 600 mg 48 Weeks**	**Any CFZ533 600 mg**	**Any CFZ533**
Arm/Group Description	Cohort 1: CFZ533 600 mg 24 Weeks	Cohort 1: CFZ533 150 mg 48 Weeks	Cohort 1: CFZ533 300 mg 48 Weeks	Cohort 1: CFZ533 600 mg 48 Weeks	All participants from cohort 1 who received CFZ533 600 mg in all Study Periods (including placebo patients who switched to CFZ533 600 mg at Week 24)	All participants from cohort 1 who received a dose of CFZ533 during the study
Number of Participants Analyzed [units: participants]	41	44	42	44	85	171
Cohort 1: Incidence of adverse events (AEs), serious adverse events (SAEs) in all Study Periods (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Death	0 (%)	0 (%)	1 (2.38%)	0 (%)	0 (%)	1 (.58%)
Adverse Event	34 (82.93%)	40 (90.91%)	38 (90.48%)	43 (97.73%)	77 (90.59%)	155 (90.64%)
Serious Adverse Event	4 (9.76%)	6 (13.64%)	6 (14.29%)	6 (13.64%)	10 (11.76%)	22 (12.87%)

AE leading to study medication discontinuation	0 (%)	2 (4.55%)	3 (7.14%)	5 (11.36%)	5 (5.88%)	10 (5.85%)

Cohort 2: Incidence of adverse events (AEs), serious adverse events (SAEs) up to Week 24

Description	The distribution of adverse events was done via the analysis of frequencies for treatment emergent Adverse Event (TEAEs), Serious Adverse Event (TESAEs) and Deaths due to AEs, through the monitoring of relevant clinical and laboratory safety parameters. Analyses of data in the Safety Set (SAF) up to Week 24 (Period 1) is presented by actual treatment during Period 1, with data from separate cohort for the CFZ533 600mg and for the Placebo groups: CFZ533 600 mg and placebo.
Time Frame	Up to Week 24
Analysis Population Description	Safety Set (SAF).

	Cohort 2: Placebo	**Cohort 2: CFZ533 600 mg**
Arm/Group Description	Cohort 2: Placebo	Cohort 2: CFZ533 600 mg
Number of Participants Analyzed [units: participants]	50	50
Cohort 2: Incidence of adverse events (AEs), serious adverse events (SAEs) up to Week 24 (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Death	0 (%)	0 (%)
Adverse Event	32 (64%)	41 (82%)
Serious Adverse Event	2 (4%)	2 (4%)
AE leading to study medication discontinuation	3 (6%)	1 (2%)

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Cohort 2: Incidence of adverse events (AEs), serious adverse events (SAEs) in all Study Periods

Description	The distribution of adverse events was done via the analysis of frequencies for treatment emergent Adverse Event (TEAEs), Serious Adverse Event (TESAEs) and Deaths due to AEs, through the monitoring of relevant clinical and laboratory safety parameters. Analyses of data in the Safety Set (SAF) for period 2/3 or overall study is presented by actual treatment sequence during periods 1 and 2, where the CFZ533 600 mg – CFZ533 600 mg sequence included data from patients in separate cohort. CFZ533 300 mg 24 Weeks includes only patients from Placebo - CFZ533 300 mg arm, who received Placebo in Period 1, and either took CFZ533 600 mg loading dose + at least two CFZ533 300 mg subsequent doses in Period 2 or missed CFZ533 600 mg loading dose and took at least one CFZ533 300 mg dose in Period 2 (Patients who received Placebo in Period 1 and discontinued before Week24 are not included). CFZ533 600 mg 48 Weeks arm includes all subjects from CFZ533 600 mg - CFZ533 600 mg arm.
Time Frame	up to 14 weeks following the last dose of study treatment, up to maximum Week 60
Analysis Population Description	Safety Set (SAF).

	Cohort 2: CFZ533 300 mg 24 Weeks	**Cohort 2: CFZ533 600 mg 48 Weeks**	**Any CFZ533**
Arm/Group Description	Cohort 2: CFZ533 300 mg 24 Weeks	Cohort 2: CFZ533 600 mg 48 Weeks	All participants from cohort 2 who received a dose of CFZ533 during the study
Number of Participants Analyzed [units: participants]	44	50	94
Cohort 2: Incidence of adverse events (AEs), serious adverse events (SAEs) in all Study Periods (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Death	0 (%)	1 (2%)	1 (1.06%)
Adverse Event	35 (79.55%)	44 (88%)	79 (84.04%)
Serious Adverse Event	5 (11.36%)	6 (12%)	11 (11.7%)
AE leading to study medication discontinuation	0 (%)	3 (6%)	3 (3.19%)

Cohort 1: Change from Baseline in Serum Free Light Kappa (FLCκ) chains levels

Description	Serum samples for free light kappa (FLCκ) chains were collected and analyzed.
Time Frame	Baseline, Week 4, Week 12, Week 24 (End Treatment Period 1), Week 32, Week 40, Week 48 (End Treatment Period 2), FUP2 (Week 56), FUP 3 (Week 60)
Analysis Population Description	Full Analysis Set. Only participants in cohort 1 with a value at both Baseline and post-baseline visit included.

	Cohort 1: Placebo - CFZ533 600 mg	**Cohort 1: CFZ533 150 mg - CFZ533 150 mg**	**Cohort 1: CFZ533 300 mg - CFZ533 300 mg**	**Cohort 1: CFZ533 600 mg - CFZ533 600 mg**
Arm/Group Description	Cohort 1: Placebo - CFZ533 600 mg	Cohort 1: CFZ533 150 mg - CFZ533 150 mg	Cohort 1: CFZ533 300 mg - CFZ533 300 mg	Cohort 1: CFZ533 600 mg - CFZ533 600 mg
Number of Participants Analyzed [units: participants]	42	41	41	38
Cohort 1: Change from Baseline in Serum Free Light Kappa (FLCκ) chains levels (units: mg/L)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Week 4	-1.9 ± 1.85	-7.2 ± 1.86	-5.4 ± 1.86	-5.5 ± 1.92
Week 12	-1.1 ± 2.02	-9.7 ± 2.01	-8.8 ± 2.03	-8.6 ± 2.08
Week 24 (End Treatment Period 1)	0.2 ± 2.26	-9.9 ± 2.26	-10.1 ± 2.28	-11.3 ± 2.35
Week 32	-8.6 ± 2.17	-11.8 ± 2.17	-11.1 ± 2.18	-8.9 ± 2.26
Week 40	-11.3 ± 2.05	-12.0 ± 2.06	-13.5 ± 2.07	-11.0 ± 2.13
Week 48 (End Treatment Period 2)	-13.9 ± 2.25	-12.5 ± 2.25	-13.1 ± 2.27	-11.6 ± 2.32
FUP2 (Week 56)	-11.8 ± 2.03	-5.6 ± 1.99	-8.9 ± 2.01	-12.4 ± 2.06
FUP 3 (Week 60)	-9.3 ± 2.07	-3.9 ± 2.04	-4.1 ± 2.07	-10.3 ± 2.11

Cohort 2: Change from Baseline in Serum Free Light Kappa (FLCκ) chains levels

Description	Serum samples for free light kappa (FLCκ) chains were collected and analyzed.

Time Frame	Baseline, Week 4, Week 12, Week 24 (End Treatment Period 1), Week 32, Week 40, Week 48 (End Treatment Period 2), FUP2 (Week 56), FUP 3 (Week 60)
Analysis Population Description	Full Analysis Set. Only participants in cohort 2 with a value at both Baseline and post-baseline visit included.

	Cohort 2: Placebo - CFZ533 300 mg	**Cohort 2: CFZ533 600 mg - CFZ533 600 mg**
Arm/Group Description	Cohort 2: Placebo - CFZ533 300 mg	Cohort 2: CFZ533 600 mg - CFZ533 600 mg
Number of Participants Analyzed [units: participants]	46	49
Cohort 2: Change from Baseline in Serum Free Light Kappa (FLCκ) chains levels (units: mg/L)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Week 4	0.3 ± 0.92	-4.3 ± 0.87
Week 12	0.1 ± 1.10	-7.2 ± 1.06
Week 24 (End Treatment Period 1)	-0.2 ± 0.90	-9.9 ± 0.86
Week 32	-6.0 ± 0.93	-10.5 ± 0.89
Week 40	-7.8 ± 0.93	-9.9 ± 0.91
Week 48 (End Treatment Period 2)	-9.3 ± 0.95	-11.9 ± 0.92
FUP2 (Week 56)	-6.1 ± 1.00	-11.7 ± 0.99
FUP 3 (Week 60)	-1.9 ± 1.11	-11.0 ± 1.09

Cohort 1: Change from Baseline in Immunoglobulin G (IgG) levels

Description	Plasma samples for Immunoglobulin G (IgG) were collected and analyzed.
Time Frame	Baseline, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24 (End Treatment Period 1), Week 28, Week 32, Week 40, Week 48 (End Treatment Period 2), FUP1 (Week 52), FUP2 (Week 56), FUP 3 (Week 60)

Analysis Population Description: Full Analysis Set. Only participants in Cohort 1 with a value at both Baseline and post-baseline visit included.

	Cohort 1: Placebo - CFZ533 600 mg	**Cohort 1: CFZ533 150 mg - CFZ533 150 mg**	**Cohort 1: CFZ533 300 mg - CFZ533 300 mg**	**Cohort 1: CFZ533 600 mg - CFZ533 600 mg**
Arm/Group Description	Cohort 1: Placebo - CFZ533 600 mg	Cohort 1: CFZ533 150 mg - CFZ533 150 mg	Cohort 1: CFZ533 300 mg - CFZ533 300 mg	Cohort 1: CFZ533 600 mg - CFZ533 600 mg
Number of Participants Analyzed [units: participants]	43	43	43	41
Cohort 1: Change from Baseline in Immunoglobulin G (IgG) levels (units: g/L)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Week 4	0.1 ± 0.31	-0.9 ± 0.31	-0.6 ± 0.31	-0.8 ± 0.32
Week 8	0.0 ± 0.31	-1.1 ± 0.31	-1.0 ± 0.31	-1.4 ± 0.31
Week 12	0.4 ± 0.28	-1.7 ± 0.27	-1.7 ± 0.28	-1.5 ± 0.28
Week 16	0.4 ± 0.39	-1.8 ± 0.39	-2.2 ± 0.39	-2.0 ± 0.40
Week 20	0.1 ± 0.35	-2.4 ± 0.34	-2.3 ± 0.35	-2.1 ± 0.36
Week 24 (End Treatment Period 1)	0.0 ± 0.36	-2.1 ± 0.35	-2.5 ± 0.36	-2.5 ± 0.36
Week 28	-0.9 ± 0.39	-2.3 ± 0.38	-2.7 ± 0.39	-2.9 ± 0.39
Week 32	-1.3 ± 0.36	-2.6 ± 0.36	-3.0 ± 0.36	-3.3 ± 0.37
Week 40	-2.3 ± 0.36	-2.7 ± 0.36	-3.2 ± 0.36	-3.1 ± 0.36
Week 48 (End Treatment Period 2)	-3.0 ± 0.40	-2.8 ± 0.40	-3.7 ± 0.41	-3.4 ± 0.40
FUP1 (Week 52)	-3.6 ± 0.47	-2.9 ± 0.46	-3.8 ± 0.47	-3.7 ± 0.46
FUP2 (Week 56)	-3.0 ± 0.45	-2.0 ± 0.43	-3.2 ± 0.44	-3.9 ± 0.44
FUP 3 (Week 60)	-2.9 ± 0.47	-1.2 ± 0.46	-1.9 ± 0.47	-3.3 ± 0.46

Cohort 2: Change from Baseline in Immunoglobulin G (IgG) levels

Description	Plasma samples for Immunoglobulin G (IgG) were collected and analyzed.
Time Frame	Baseline, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24 (End Treatment Period 1), Week 28, Week 32, Week 40, Week 48 (End Treatment Period 2), FUP1 (Week 52), FUP2 (Week 56), FUP 3 (Week 60)
Analysis Population Description	Full Analysis Set. Only participants in cohort 2 with a value at both Baseline and post-baseline visit included.

	Cohort 2: Placebo - CFZ533 300 mg	**Cohort 2: CFZ533 600 mg - CFZ533 600 mg**
Arm/Group Description	Cohort 2: Placebo - CFZ533 300 mg	Cohort 2: CFZ533 600 mg - CFZ533 600 mg
Number of Participants Analyzed [units: participants]	47	49
Cohort 2: Change from Baseline in Immunoglobulin G (IgG) levels (units: g/L)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Week 4	-0.8 ± 0.25	-0.8 ± 0.24
Week 8	-0.5 ± 0.28	-1.9 ± 0.27
Week 12	-0.4 ± 0.30	-2.5 ± 0.29
Week 16	-0.6 ± 0.32	-3.0 ± 0.30
Week 20	-0.7 ± 0.32	-3.2 ± 0.30
Week 24 (End Treatment Period 1)	0.0 ± 0.42	-3.6 ± 0.40
Week 28	-1.3 ± 0.38	-4.2 ± 0.36
Week 32	-1.5 ± 0.35	-4.1 ± 0.34
Week 40	-2.6 ± 0.43	-4.9 ± 0.42
Week 48 (End Treatment Period 2)	-3.2 ± 0.43	-4.5 ± 0.43
FUP1 (Week 52)	-4.0 ± 0.45	-5.0 ± 0.44
FUP2 (Week 56)	-3.3 ± 0.46	-4.8 ± 0.45
FUP 3 (Week 60)	-2.4 ± 0.46	-4.5 ± 0.45

Cohort 1: Change from Baseline in Immunoglobulin M (IgM) levels

Description	Plasma samples for Immunoglobulin M (IgM) were collected and analyzed.
Time Frame	Baseline, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24 (End Treatment Period 1), Week 28, Week 32, Week 40, Week 48 (End Treatment Period 2), FUP1 (Week 52), FUP2 (Week 56), FUP 3 (Week 60)
Analysis Population Description	Full Analysis Set. Only participants in cohort 1 with a value at both Baseline and post-baseline visit included.

	Cohort 1: Placebo - CFZ533 600 mg	**Cohort 1: CFZ533 150 mg - CFZ533 150 mg**	**Cohort 1: CFZ533 300 mg - CFZ533 300 mg**	**Cohort 1: CFZ533 600 mg - CFZ533 600 mg**
Arm/Group Description	Cohort 1: Placebo - CFZ533 600 mg	Cohort 1: CFZ533 150 mg - CFZ533 150 mg	Cohort 1: CFZ533 300 mg - CFZ533 300 mg	Cohort 1: CFZ533 600 mg - CFZ533 600 mg
Number of Participants Analyzed [units: participants]	43	43	43	41
Cohort 1: Change from Baseline in Immunoglobulin M (IgM) levels (units: g/L)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Week 4	0.0 ± 0.04	-0.1 ± 0.04	-0.1 ± 0.04	-0.1 ± 0.04
Week 8	0.0 ± 0.04	-0.2 ± 0.04	-0.3 ± 0.04	-0.2 ± 0.04
Week 12	0.0 ± 0.04	-0.2 ± 0.04	-0.3 ± 0.04	-0.2 ± 0.04
Week 16	0.0 ± 0.05	-0.2 ± 0.05	-0.3 ± 0.05	-0.3 ± 0.05
Week 20	0.0 ± 0.05	-0.2 ± 0.05	-0.4 ± 0.05	-0.3 ± 0.05
Week 24 (End Treatment Period 1)	0.0 ± 0.06	-0.2 ± 0.06	-0.4 ± 0.06	-0.3 ± 0.06
Week 28	-0.1 ± 0.05	-0.2 ± 0.05	-0.4 ± 0.05	-0.3 ± 0.05
Week 32	-0.2 ± 0.06	-0.2 ± 0.06	-0.4 ± 0.06	-0.3 ± 0.06
Week 40	-0.3 ± 0.06	-0.2 ± 0.06	-0.4 ± 0.06	-0.3 ± 0.06
Week 48 (End Treatment Period 2)	-0.3 ± 0.06	-0.2 ± 0.06	-0.4 ± 0.06	-0.3 ± 0.06

FUP1 (Week 52)	-0.4 ± 0.05	-0.2 ± 0.05	-0.4 ± 0.05	-0.3 ± 0.05
FUP2 (Week 56)	-0.3 ± 0.05	0.0 ± 0.05	-0.1 ± 0.05	-0.3 ± 0.05
FUP 3 (Week 60)	-0.2 ± 0.07	-0.1 ± 0.06	0.0 ± 0.07	-0.2 ± 0.06

Cohort 2: Change from Baseline in Immunoglobulin M (IgM) levels

Description	Plasma samples for Immunoglobulin M (IgM) were collected and analyzed.
Time Frame	Baseline, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24 (End Treatment Period 1), Week 28, Week 32, Week 40, Week 48 (End Treatment Period 2), FUP1 (Week 52), FUP2 (Week 56), FUP 3 (Week 60)
Analysis Population Description	Full Analysis Set. Only participants in cohort 2 with a value at both Baseline and post-baseline visit included.

	Cohort 2: Placebo - CFZ533 300 mg	**Cohort 2: CFZ533 600 mg - CFZ533 600 mg**
Arm/Group Description	Cohort 2: Placebo - CFZ533 300 mg	Cohort 2: CFZ533 600 mg - CFZ533 600 mg
Number of Participants Analyzed [units: participants]	47	49
Cohort 2: Change from Baseline in Immunoglobulin M (IgM) levels (units: g/L)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Week 4	0.0 ± 0.03	-0.1 ± 0.03
Week 8	0.0 ± 0.04	-0.3 ± 0.04
Week 12	0.0 ± 0.05	-0.3 ± 0.05
Week 16	-0.1 ± 0.06	-0.4 ± 0.05
Week 20	-0.1 ± 0.06	-0.4 ± 0.06
Week 24 (End Treatment Period 1)	0.0 ± 0.06	-0.4 ± 0.06
Week 28	-0.2 ± 0.06	-0.5 ± 0.06
Week 32	-0.2 ± 0.07	-0.5 ± 0.06

Week 40	-0.3 ± 0.07	-0.5 ± 0.07
Week 48 (End Treatment Period 2)	-0.3 ± 0.07	-0.5 ± 0.07
FUP1 (Week 52)	-0.3 ± 0.06	-0.5 ± 0.06
FUP2 (Week 56)	-0.2 ± 0.72	-0.5 ± 0.07
FUP 3 (Week 60)	-0.1 ± 0.08	-0.5 ± 0.08

Cohort 1: Change from Baseline in plasma CXCL-13 levels

Description	Plasma samples for Chemokine (C-X-C motif) ligand 13 (CXCL13), also known as B lymphocyte chemoattractant (BLC) or B cell-attracting chemokine 1 (BCA-1) were collected and analyzed.
Time Frame	Baseline, Week 4, Week 12, Week 24 (End Treatment Period 1), Week 32, Week 48 (End Treatment Period 2), FUP 3 (Week 60)
Analysis Population Description	Full Analysis Set. Only participants in cohort 1 with a value at both Baseline and post-baseline visit included.

	Cohort 1: Placebo - CFZ533 600 mg	**Cohort 1: CFZ533 150 mg - CFZ533 150 mg**	**Cohort 1: CFZ533 300 mg - CFZ533 300 mg**	**Cohort 1: CFZ533 600 mg - CFZ533 600 mg**
Arm/Group Description	Cohort 1: Placebo - CFZ533 600 mg	Cohort 1: CFZ533 150 mg - CFZ533 150 mg	Cohort 1: CFZ533 300 mg - CFZ533 300 mg	Cohort 1: CFZ533 600 mg - CFZ533 600 mg
Number of Participants Analyzed [units: participants]	43	40	41	39
Cohort 1: Change from Baseline in plasma CXCL-13 levels (units: pg/mL)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Week 4	-19.0 ± 12.51	-78.7 ± 12.84	-88.4 ± 12.74	-77.0 ± 13.23
Week 12	-23.8 ± 12.42	-99.4 ± 12.56	-77.4 ± 12.59	-108.5 ± 12.69
Week 24 (End Treatment Period 1)	-15.6 ± 13.78	-89.7 ± 14.08	-83.2 ± 13.98	-111.6 ± 14.26
Week 32	-102.5 ± 17.37	-80.5 ± 17.68	-78.3 ± 18.21	-71.3 ± 19.02
Week 48 (End Treatment Period 2)	-116.6 ± 11.73	-75.9 ± 12.02	-89.7 ± 12.26	-118.7 ± 12.15

FUP 3 (Week 60)	-73.9 ± 21.62	24.4 ± 22.10	-22.4 ± 22.55	-68.7 ± 22.24

Cohort 2: Change from Baseline in plasma CXCL-13 levels

Description	Plasma samples for Chemokine (C-X-C motif) ligand 13 (CXCL13), also known as B lymphocyte chemoattractant (BLC) or B cell-attracting chemokine 1 (BCA-1) were collected and analyzed.
Time Frame	Baseline, Week 4, Week 12, Week 24 (End Treatment Period 1), Week 32, Week 48 (End Treatment Period 2), FUP 3 (Week 60)
Analysis Population Description	Full Analysis Set. Only participants in cohort 2 with a value at both Baseline and post-baseline visit included.

	Cohort 2: Placebo - CFZ533 300 mg	**Cohort 2: CFZ533 600 mg - CFZ533 600 mg**
Arm/Group Description	Cohort 2: Placebo - CFZ533 300 mg	Cohort 2: CFZ533 600 mg - CFZ533 600 mg
Number of Participants Analyzed [units: participants]	45	49
Cohort 2: Change from Baseline in plasma CXCL-13 levels (units: pg/mL)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Week 4	-9.0 ± 8.50	-88.7 ± 7.99
Week 12	8.8 ± 16.16	-97.8 ± 15.55
Week 24 (End Treatment Period 1)	-27.4 ± 7.19	-114.1 ± 6.81
Week 32	-97.2 ± 7.03	-116.1 ± 6.65
Week 48 (End Treatment Period 2)	-99.2 ± 6.84	-107.8 ± 6.81
FUP 3 (Week 60)	-10.9 ± 10.76	-66.5 ± 10.53

Other Pre-Specified Outcome Result(s)

No data identified.

Post-Hoc Outcome Result(s)

No data identified.

Safety Results

Time Frame	On-treatment adverse events and deaths were reported from first dose of study treatment to 14 weeks after last dose of study medication, up to Week 60.
Additional Description	Any sign or symptom that occurred during the conduct of the trial and safety follow-up. The safety analysis were done on the safety population, which included all randomized subjects who received at least one dose of study medication. Patients were analyzed according to the actual treatment received.
Source Vocabulary for Table Default	MedDRA (26.0)
Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	Cohort 1 / Arm D (Period 1): Placebo N = 43	Cohort 1 / Arm D1 (Period 2): CFZ533 600mg (from Week 24) N = 41	Cohort 1/Arm C: CFZ533 150 mg N = 44	Cohort 1/Arm B: CFZ533 300 mg N = 42	Cohort 1/Arm A: CFZ533 600 mg N = 44	Cohort 2/Arm F: Placebo N = 50	Cohort 2 / Arm F1 (Period 2): CFZ533 300mg N = 44	Cohort 2/Arm E: CFZ533 600 mg N = 50
Arm/Group Description	Placebo treatment is administered subcutaneous (s.c.) weekly for the first 3	3 weekly subcutaneous (s.c.) loading doses of 600 mg iscalimab on Week 24,	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg	Placebo treatment was administered subcutaneous (s.c.) weekly for the first 3	3 weekly subcutaneous (s.c.) loading doses of iscalimab: 600 mg on Week	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg

	doses, then bi-weekly from Week 2 to Week 22 in Period 1.	25 and 26. After Week 26 and up to Week 46 (last dose), iscalimab was administered bi-weekly at 600 mg.	on Week 0, and 150 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 150 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	on Week 0, and 300 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 300 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	on Weeks 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	doses, then bi-weekly from Week 2 to Week 22 in Period 1.	24, and 300 mg on Week 25 and Week 26. After Week 26, iscalimab was administered s.c. bi-weekly at 300 mg.	on Week 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.
Total Number Affected	0	0	0	1	0	0	0	1
Total Number At Risk	43	41	44	42	44	50	44	50

Serious Adverse Events

Time Frame	On-treatment adverse events and deaths were reported from first dose of study treatment to 14 weeks after last dose of study medication, up to Week 60.
Additional Description	Any sign or symptom that occurred during the conduct of the trial and safety follow-up. The safety analysis were done on the safety population, which included all randomized subjects who received at least one dose of study medication. Patients were analyzed according to the actual treatment received.
Source Vocabulary for Table Default	MedDRA (26.0)

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Collection Approach for Table Default Systematic Assessment

	Cohort 1 / Arm D (Period 1): Placebo N = 43	Cohort 1 / Arm D1 (Period 2): CFZ533 600mg (from Week 24) N = 41	Cohort 1/Arm C: CFZ533 150 mg N = 44	Cohort 1/Arm B: CFZ533 300 mg N = 42	Cohort 1/Arm A: CFZ533 600 mg N = 44	Cohort 2/Arm F: Placebo N = 50	Cohort 2 / Arm F1 (Period 2): CFZ533 300mg N = 44	Cohort 2/Arm E: CFZ533 600 mg N = 50
Arm/Group Description	Placebo treatment is administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2 to Week 22 in Period 1.	3 weekly subcutaneous (s.c.) loading doses of 600 mg iscalimab on Week 24, 25 and 26. After Week 26 and up to Week 46 (last dose), iscalimab was administered bi-weekly at 600 mg.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 150 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 150 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 300 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 300 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Weeks 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	Placebo treatment was administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2 to Week 22 in Period 1.	3 weekly subcutaneous (s.c.) loading doses of iscalimab: 600 mg on Week 24, and 300 mg on Week 25 and Week 26. After Week 26, iscalimab was administered s.c. bi-weekly at 300 mg.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.

Total # Affected by any Serious Adverse Event	1	4	6	6	6	2	5	6
Total # at Risk by any Serious Adverse Event	43	41	44	42	44	50	44	50
Blood and lymphatic system disorders								
Anaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.27%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cardiac disorders								
Angina pectoris	0 (0.00%)	0 (0.00%)	1 (2.27%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Arteriosclerosis coronary artery	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.27%)	0 (0.00%)
Cardiac failure congestive	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.00%)
Ear and labyrinth disorders								
Vertigo	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.00%)	0 (0.00%)	0 (0.00%)
Eye disorders								
Angle closure glaucoma	0 (0.00%)	0 (0.00%)	1 (2.27%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrointestinal disorders								
Enteritis	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Haematochezia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pancreatitis acute	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Salivary gland cyst	0 (0.00%)	0 (0.00%)	1 (2.27%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

General disorders and administration site conditions								
Pyrexia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.00%)
Hepatobiliary disorders								
Cholecystitis	0 (0.00%)	1 (2.44%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infections and infestations								
Appendicitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.27%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
COVID-19	0 (0.00%)	0 (0.00%)	1 (2.27%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.00%)
Laryngitis bacterial	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.00%)	0 (0.00%)	0 (0.00%)
Lower respiratory tract infection	0 (0.00%)	0 (0.00%)	1 (2.27%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Meningitis aseptic	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.00%)
Pneumocystis jirovecii pneumonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pneumonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	1 (2.27%)	1 (2.00%)
Postoperative wound infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.27%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory tract infection viral	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.27%)	0 (0.00%)
Retroperitoneal abscess	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.27%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tuberculosis	0 (0.00%)	1 (2.44%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Wound abscess	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.27%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Injury, poisoning and procedural complications								
Ankle fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Fibula fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.27%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tibia fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.27%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Musculoskeletal and connective tissue disorders								
Hand deformity	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.00%)
Osteoarthritis	0 (0.00%)	1 (2.44%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Sjogren's syndrome	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.27%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)								
Bladder cancer	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.27%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Breast cancer	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.27%)	1 (2.00%)
Nervous system disorders								
Cerebrovascular disorder	0 (0.00%)	0 (0.00%)	1 (2.27%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dizziness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.27%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Migraine	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Transient ischaemic attack	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.00%)
Renal and urinary disorders								
Glomerulonephritis	1 (2.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nephrolithiasis	0 (0.00%)	1 (2.44%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Renal colic	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.27%)	0 (0.00%)
Reproductive system and breast disorders								

Pelvic organ prolapse	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.27%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders								
Dyspnoea	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypoxia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pulmonary oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory distress	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory failure	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Other (Not Including Serious) Adverse Events

Time Frame	On-treatment adverse events and deaths were reported from first dose of study treatment to 14 weeks after last dose of study medication, up to Week 60.
Additional Description	Any sign or symptom that occurred during the conduct of the trial and safety follow-up. The safety analysis were done on the safety population, which included all randomized subjects who received at least one dose of study medication. Patients were analyzed according to the actual treatment received.
Source Vocabulary for Table Default	MedDRA (26.0)
Collection Approach for Table Default	Systematic Assessment

Frequent Event Reporting Threshold 5%

	Cohort 1 / Arm D (Period 1): Placebo N = 43	Cohort 1 / Arm D1 (Period 2): CFZ533 600mg (from Week 24) N = 41	Cohort 1/Arm C: CFZ533 150 mg N = 44	Cohort 1/Arm B: CFZ533 300 mg N = 42	Cohort 1/Arm A: CFZ533 600 mg N = 44	Cohort 2/Arm F: Placebo N = 50	Cohort 2 / Arm F1 (Period 2): CFZ533 300mg N = 44	Cohort 2/Arm E: CFZ533 600 mg N = 50
Arm/Group Description	Placebo treatment is administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2 to Week 22 in Period 1.	3 weekly subcutaneous (s.c.) loading doses of 600 mg iscalimab on Week 24, 25 and 26. After Week 26 and up to Week 46 (last dose), iscalimab was administered bi-weekly at 600 mg.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 150 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 150 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, and 300 mg on Week 1 and Week 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 300 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Weeks 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.	Placebo treatment was administered subcutaneous (s.c.) weekly for the first 3 doses, then bi-weekly from Week 2 to Week 22 in Period 1.	3 weekly subcutaneous (s.c.) loading doses of iscalimab: 600 mg on Week 24, and 300 mg on Week 25 and Week 26. After Week 26, iscalimab was administered s.c. bi-weekly at 300 mg.	3 weekly subcutaneous (s.c.) loading doses of iscalimab were 600 mg on Week 0, 1 and 2. From Week 2 and up to Week 46 (last dose), iscalimab was administered s.c. bi-weekly at 600 mg. To maintain blinding in Period 2, placebo was administered at Week 25.
Total # Affected by any Other Adverse Event	18	28	33	34	34	27	32	41
Total # at Risk by any Other Adverse Event	43	41	44	42	44	50	44	50

Blood and lymphatic system disorders								
Iron deficiency anaemia	1 (2.33%)	1 (2.44%)	1 (2.27%)	0 (0.00%)	1 (2.27%)	1 (2.00%)	1 (2.27%)	3 (6.00%)
Leukopenia	0 (0.00%)	1 (2.44%)	0 (0.00%)	3 (7.14%)	2 (4.55%)	0 (0.00%)	0 (0.00%)	2 (4.00%)
Neutropenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	5 (11.90%)	2 (4.55%)	0 (0.00%)	0 (0.00%)	1 (2.00%)
Ear and labyrinth disorders								
Vertigo	0 (0.00%)	1 (2.44%)	1 (2.27%)	0 (0.00%)	1 (2.27%)	0 (0.00%)	1 (2.27%)	3 (6.00%)
Endocrine disorders								
Thyroid mass	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.27%)	3 (6.00%)
Gastrointestinal disorders								
Abdominal pain	0 (0.00%)	0 (0.00%)	1 (2.27%)	1 (2.38%)	4 (9.09%)	1 (2.00%)	1 (2.27%)	2 (4.00%)
Abdominal pain upper	2 (4.65%)	0 (0.00%)	1 (2.27%)	4 (9.52%)	0 (0.00%)	0 (0.00%)	2 (4.55%)	2 (4.00%)
Diarrhoea	1 (2.33%)	1 (2.44%)	2 (4.55%)	1 (2.38%)	3 (6.82%)	5 (10.00%)	1 (2.27%)	4 (8.00%)
Nausea	0 (0.00%)	0 (0.00%)	2 (4.55%)	1 (2.38%)	2 (4.55%)	3 (6.00%)	1 (2.27%)	4 (8.00%)
Parotid gland enlargement	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (7.14%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
General disorders and administration site conditions								
Asthenia	0 (0.00%)	1 (2.44%)	1 (2.27%)	2 (4.76%)	3 (6.82%)	0 (0.00%)	0 (0.00%)	1 (2.00%)
Fatigue	1 (2.33%)	1 (2.44%)	5 (11.36%)	1 (2.38%)	3 (6.82%)	0 (0.00%)	1 (2.27%)	2 (4.00%)
Pyrexia	3 (6.98%)	2 (4.88%)	6 (13.64%)	4 (9.52%)	0 (0.00%)	0 (0.00%)	2 (4.55%)	4 (8.00%)
Infections and infestations								
Conjunctivitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.27%)	3 (6.00%)	2 (4.55%)	1 (2.00%)

COVID-19	2 (4.65%)	10 (24.39%)	10 (22.73%)	11 (26.19%)	11 (25.00%)	8 (16.00%)	8 (18.18%)	20 (40.00%)
Herpes simplex	1 (2.33%)	0 (0.00%)	4 (9.09%)	0 (0.00%)	1 (2.27%)	0 (0.00%)	0 (0.00%)	3 (6.00%)
Influenza	0 (0.00%)	3 (7.32%)	2 (4.55%)	4 (9.52%)	2 (4.55%)	0 (0.00%)	2 (4.55%)	1 (2.00%)
Nasopharyngitis	2 (4.65%)	6 (14.63%)	5 (11.36%)	8 (19.05%)	9 (20.45%)	3 (6.00%)	3 (6.82%)	6 (12.00%)
Oral herpes	2 (4.65%)	0 (0.00%)	3 (6.82%)	2 (4.76%)	5 (11.36%)	1 (2.00%)	4 (9.09%)	1 (2.00%)
Pneumonia	0 (0.00%)	0 (0.00%)	2 (4.55%)	1 (2.38%)	1 (2.27%)	0 (0.00%)	0 (0.00%)	3 (6.00%)
Rhinitis	1 (2.33%)	1 (2.44%)	0 (0.00%)	0 (0.00%)	2 (4.55%)	2 (4.00%)	1 (2.27%)	5 (10.00%)
Sinusitis	0 (0.00%)	1 (2.44%)	1 (2.27%)	2 (4.76%)	1 (2.27%)	2 (4.00%)	1 (2.27%)	4 (8.00%)
Upper respiratory tract infection	1 (2.33%)	4 (9.76%)	3 (6.82%)	3 (7.14%)	1 (2.27%)	1 (2.00%)	3 (6.82%)	6 (12.00%)
Urinary tract infection	2 (4.65%)	3 (7.32%)	3 (6.82%)	4 (9.52%)	5 (11.36%)	0 (0.00%)	4 (9.09%)	8 (16.00%)
Injury, poisoning and procedural complications								
Fall	1 (2.33%)	0 (0.00%)	3 (6.82%)	0 (0.00%)	1 (2.27%)	0 (0.00%)	1 (2.27%)	1 (2.00%)
Immunisation reaction	1 (2.33%)	3 (7.32%)	1 (2.27%)	3 (7.14%)	1 (2.27%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Musculoskeletal and connective tissue disorders								
Arthralgia	4 (9.30%)	2 (4.88%)	6 (13.64%)	2 (4.76%)	5 (11.36%)	4 (8.00%)	5 (11.36%)	5 (10.00%)
Back pain	1 (2.33%)	2 (4.88%)	4 (9.09%)	3 (7.14%)	1 (2.27%)	3 (6.00%)	6 (13.64%)	6 (12.00%)
Myalgia	1 (2.33%)	1 (2.44%)	1 (2.27%)	3 (7.14%)	2 (4.55%)	1 (2.00%)	1 (2.27%)	4 (8.00%)
Neck pain	0 (0.00%)	0 (0.00%)	1 (2.27%)	0 (0.00%)	3 (6.82%)	0 (0.00%)	2 (4.55%)	0 (0.00%)
Pain in extremity	1 (2.33%)	0 (0.00%)	1 (2.27%)	1 (2.38%)	3 (6.82%)	1 (2.00%)	2 (4.55%)	4 (8.00%)
Nervous system disorders								
Dizziness	2 (4.65%)	0 (0.00%)	2 (4.55%)	3 (7.14%)	4 (9.09%)	2 (4.00%)	2 (4.55%)	0 (0.00%)

Headache	5 (11.63%)	1 (2.44%)	9 (20.45%)	6 (14.29%)	8 (18.18%)	5 (10.00%)	4 (9.09%)	3 (6.00%)
Respiratory, thoracic and mediastinal disorders								
Cough	1 (2.33%)	1 (2.44%)	3 (6.82%)	3 (7.14%)	2 (4.55%)	2 (4.00%)	1 (2.27%)	3 (6.00%)
Oropharyngeal pain	0 (0.00%)	0 (0.00%)	2 (4.55%)	3 (7.14%)	1 (2.27%)	1 (2.00%)	0 (0.00%)	0 (0.00%)
Skin and subcutaneous tissue disorders								
Alopecia	0 (0.00%)	1 (2.44%)	0 (0.00%)	0 (0.00%)	3 (6.82%)	2 (4.00%)	0 (0.00%)	3 (6.00%)
Eczema	0 (0.00%)	0 (0.00%)	2 (4.55%)	1 (2.38%)	3 (6.82%)	2 (4.00%)	1 (2.27%)	3 (6.00%)
Pruritus	1 (2.33%)	0 (0.00%)	1 (2.27%)	0 (0.00%)	1 (2.27%)	3 (6.00%)	0 (0.00%)	3 (6.00%)
Rash	0 (0.00%)	2 (4.88%)	1 (2.27%)	2 (4.76%)	1 (2.27%)	4 (8.00%)	0 (0.00%)	6 (12.00%)
Vascular disorders								
Haematoma	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (6.82%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypertension	4 (9.30%)	0 (0.00%)	2 (4.55%)	0 (0.00%)	2 (4.55%)	3 (6.00%)	2 (4.55%)	2 (4.00%)

Other Relevant Findings

None

Conclusion:

This study met its primary objective. This study suggests a potential treatment benefit in patients with Sjögren’s syndrome.

Date of Clinical Trial Report

30-Apr-2024